Historical Feature

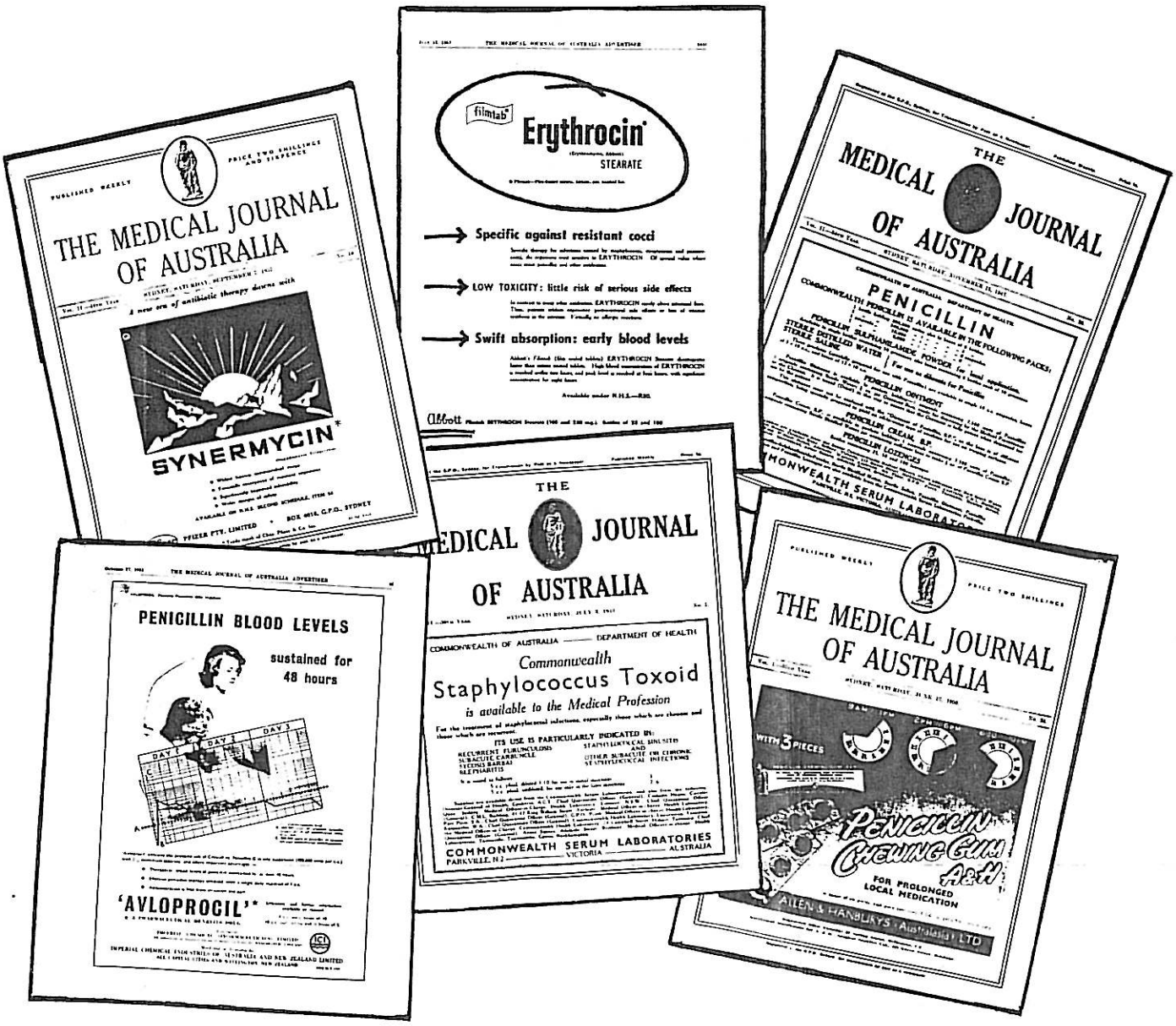
Fleeting Hopes and Promises of Advertising

WHENEVER WE PRESCRIBE a medication, we do so in the belief—acquired through clinical experience, discussions and conferences with colleagues, and the reading of medical journals and drug advertisements—that it is the latest and best available. While hoping that the problem we are dealing with may one day be prevented, we also have faith in pharmacologic research to develop new and improved drugs in the meantime.

Yet should this thinking apply equally to the use and development of antibiotic agents? In spite of worldwide concern over increasing bacterial resistance to antibiotic agents and the overuse of these medications, most issues of major medical journals (if they are not publishing reports of poor prescribing practices) publish page after page of advertisements for one or another "new" antibiotic agent, more often than not with psychedelic colours and other arty effects that make a "Star Wars" poster look like the fine print on an eye chart (my favourite: "Mega-Spectrum MEZLIN", mezlocillin sodium, advertised in the May 14 issue of JAMA).

Although methicillin may have become the latest casualty in medicine's own "Staph wars", we know there will be many others. In May, 1982, Leo Laboratories tells readers of the BMJ *and* The Lancet *(and presumably this journal as well if the company so chose), "For the treatment of staphylococcal infection fucidin (sodium fusidate) knows no barriers!" and Beecham Research Laboratories adds, "When staphylococci are involved or suspected—make Floxapen (flucloxacillin) part of the treatment". Although we realise that these medications are among the best available, it is sobering to look back at some of the transient methods we have been called upon to use over the years in the treatment of staphylococcal infections.*

—Alan Blum



favourable groups of alcoholics (such as single, divorced, or widowed men and women) is as yet unknown but may appear doubtful to the practising clinician.[3] The statement that, "Treatment may actually make some alcoholics worse" by protecting them from the consequences of their drinking or by fostering inactivity surely applies only to utterly inadequate "treatment." The risks arising from the behaviour of well-meaning "enablers" who shelter the alcoholic from experiencing the painful effects of his drinking on himself (and others) and the importance of fostering the patient's responsibility for his recovery, his own initiative, and active participation in the therapeutic programme are surely nowadays well known to every experienced therapist. The finding of some community-based studies that sociopathy did not predict outcome is surprising; it contrasts with most clinicians' observations[1-3] and also with the statement in your leading article that "the best predictor is stability in one's own job and marriage." Social stability (with its link with "good outcome") is hardly a characteristic feature of sociopathy.

M M GLATT

University College Hospital
Alcoholism Teaching Centre,
St Pancras Hospital,
London NW1

1 Glatt MM. *Br J Addict* 1955;52:55-92.
2 Glatt MM. *Lancet* 1959;ii:397-8.
3 Glatt MM. *Alcoholism*. London: Teach Yourself Books, 1982.
4 Orford J, Edwards G. *Alcoholism*. London: Oxford University Press, 1977.

Benoxaprofen

SIR,—In analysing the suspension of the product licence of a drug linked to at least 61 deaths and 3500 adverse reactions in the past two years, the author of your leading article (14 August, p 459) has raised serious but necessary questions about the roles of the manufacturer, pharmaceutical companies in general, the Committee on Safety of Medicines, the lay press, practising doctors, and even the public at large. No mention was made, however, of the role of editors and advertising managers of medical journals, under whose aegis Opren (benoxaprofen) was provided with a credible context from the outset.

The influence of pharmaceutical advertising directed at prescribing doctors—and the responsibility of those persons at medical journals who approve an advertisement for publication—must also be considered. In this instance, two-page and three-page advertisements for benoxaprofen appeared prominently in no fewer than 20 issues of the *BMJ* alone in the two years since the introduction of the drug. One such advertisement favourably compared the five-letter brand-name product with the more unwieldy generic name counterparts: diclofenac, flurbiprofen, indomethacin, and piroxicam. As in many pharmaceutical advertisements, the prescribing information was obscurely placed, and included vague sentences such as "Peptic ulceration has occured (sic) only rarely."

Practising doctors and medical editors alike may resent the implication that frequency and prominence of advertisements for a drug increase the number of prescriptions. I believe most doctors would say they pay little attention to the advertisements, much less prescribe a drug on the basis of one. None the less, the irony is inescapable that while manuscripts, including those dealing with clinical drug trials and post-marketing surveillance programmes, often undergo extensive revision before acceptance for publication, paid advertisements extolling only the virtues of various products generally are accepted without modification.

In the face of the need to maintain fiscal viability while upholding the highest editorial standards, what is a medical journal to do in regard to advertising? The issue needs to be explored by both editors and medical associations at their meetings. One proposal has been raised[1] and seconded[2] for a "physician boycott" of drugs that are unethically promoted. Alternatively, I would propose that medical journals reject advertising for prescription products that are also promoted and advertised in the lay press. In addition, as a way of discouraging the rush to prescribe new drugs, I would propose that journals either wait for a period of time after the introduction of a drug before accepting an advertisement for it, or confine the content of the advertisements to prescribing information.

In my opinion, the benoxaprofen affair points out the need for more careful "peer review" by medical editors and other doctors of pharmaceutical advertisements submitted for publication.

ALAN BLUM
Editor

Medical Journal of Australia,
Glebe,
New South Wales,
Australia 2037

1 Solomon SD, Grimmett BL, Maurer KH, Levin NW. *N Engl J Med* 1979;300:203.
2 Mallace AH. *N Engl J Med* 1979;300:734.

**The *BMJ* has a code which it applies to all advertisements; the prime requirement is that: "Statements of fact should be supported by trustworthy evidence." We do reject advertisements or ask the advertiser to modify the wording or presentation on grounds of accuracy or taste. For us to object to an advertisement on the grounds of frequency would, however, be unduly quixotic.—ED, *BMJ*.

SIR,—While we generally agree with the thoughtful leading article on benoxaprofen (14 August, p 459), there is one correction which is germane to your query as to whether the Committee on Safety of Medicines acted too slowly in banning the drug.

In a letter to the *BMJ* (29 May, p 1630) Lilly vice-president Ian Shedden stated that "no jaundice" had been seen "in approximately 2200 carefully followed patients who participated in clinical trials in the USA." This statement is repeated in the leading article. In fact five cases of reversible jaundice, including four cases with concomitant (also reversible) renal disease, occurred in patients in US clinical trials prior to the US marketing of benoxaprofen in May 1982.[1] The first case occurred in 1978.

Although the US cases occurred in younger patients, they bear a striking similarity to many of the fatal cases reported in the UK. Until we know whether Lilly informed the Committee on Safety of Medicines promptly about these cases, we cannot determine whether the Committee on Safety of Medicines acted too slowly in banning benoxaprofen.

The best mechanism for early warning of side effects, especially those occurring more frequently than once in a thousand patients, is the carefully controlled and monitored clinical trial. Unless there is prompt reporting of the results of such trials by the sponsoring drug company to all governmental agencies in countries marketing or planning to market a particular drug, the Committee on Safety of Medicines, the Food and Drug Administration, and similar agencies in other countries will not be acting on the best available information.

SIDNEY M WOLFE
EVE BARGMANN

Health Research Group,
Washington DC 20036

1 July 2, 1982. Submission by Lilly to the Food and Drug Administration.

Prescription-event monitoring

**The following is a draft of a letter to be sent to all GPs in England.—ED, *BMJ*.

SIR,—In my letter of 26 February this year I described the preliminary results of our pilot study of prescription-event monitoring. Your response was excellent and I felt that the rapid feedback, less than one month after the "green forms" had been distributed, would be appreciated. Although this was only a small-scale study designed to test the system, some interesting and fairly reassuring data on the two drugs—fenbufen (Lederfen) and benoxaprofen (Opren)—were also obtained.

Among approximately 6000 green forms returned for benoxaprofen, there were eight in which jaundice had been reported as an "event." Further inquiries eliminated some patients with alternative causes and others who were not taking the drug, and there remained only three cases in which benoxaprofen was a possible cause. Prescription-event monitoring had thus signalled a potential risk, but I considered that these few reports did not justify raising an alarm, at least until the hypothesis had been tested in a larger series.

Four months later, a small cluster of reports of benoxaprofen-associated jaundice appeared in the journals. They tended to strengthen our earlier signal, and defined the problem as one which mainly affected elderly patients. The manufacturers circulated a warning to prescribers on 21 June recommending that elderly patients should take no more than 300 mg daily. On 3 August, it was announced that the licence for benoxaprofen had been temporarily suspended by the Department of Health and Social Security.

The following preliminary statistics from the pilot study may be of interest:

(1) Ninety-five per cent of benoxaprofen and 96% of fenbufen patients had been prescribed daily doses of 600 mg or more.

(2) Fifty-six per cent of both groups had been treated for osteoarthritis. Twenty per cent of the benoxaprofen and 11% of the fenbufen group had been treated for rheumatoid arthritis.

(3) Thirty-six per cent of the benoxaprofen group were under 60 years of age, 29% were aged 60-69, and 35% were over 70. Corresponding figures for fenbufen were 33%, 25%, and 42% respectively.

(4) About 40% of patients on benoxaprofen and 43% of those on fenbufen continued their treatment beyond the 12 months of the study. Of the remainder, the mean duration of treatment was approximately 18 weeks for benoxaprofen and 15 weeks for fenbufen.

(5) In both groups the overall mortality during the 12 months of the study was 3%.

Excepting that relatively fewer patients with rheumatoid arthritis were treated with fenbufen, the two groups were very similar in other respects. Although the questionnaires were not designed to test efficacy, a number of doctors volunteered the information that patients taking benoxaprofen